**Supplemental digital content 1. Illustrates the standardized case record form (CRF).**

**Title: Classification of Death Causes after Transplantation (CLASS): evaluation of methodology and initial results.**

**1. author: Neval Ete Wareham**

**Supplemental digital content 1**

**Section 1 Background, clinical and demographics**

A. Year of birth: B. Gender: male female

C. Transplant date: D. Transplant type:

E. Primary disease: F: Prior transplantations: yes no date:

**Section 2 Risk factors (please mark all that apply)**

**A. Ongoing risk factors in the year prior to death:**

 1. Cigarette smoking \_\_\_ Yes \_\_\_No \_\_Unknown

 2. Excessive alcohol consumption \_\_\_ Yes \_\_\_No \_\_Unknown

 3. Active illicit injecting drug use \_\_\_ Yes \_\_\_No \_\_Unknown

 4. Active illicit non-injecting drug use \_\_\_ Yes \_\_\_No \_\_Unknown

 5. Opiate substitution \_\_\_ Yes \_\_\_No \_\_Unknown

**Section 3 Co-morbidities (please mark all that apply)**

**A. Ongoing chronic conditions:**

1. DM \_\_\_ Yes \_\_\_No \_\_Unknown

 2. Hypertension \_\_\_ Yes \_\_\_No \_\_Unknown

 3. Dyslipidemia \_\_\_ Yes \_\_\_No \_\_Unknown

**B. Prior cardiovascular disease** \_\_\_ Yes \_\_\_No \_\_Unknown

**If yes, please specify disease:** ­­­­­­­­­­­­­­­­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**C. Prior peripheral arterial disease** \_\_\_ Yes \_\_\_No \_\_Unknown

**If yes, please specify disease:** ­­­­­­­­­­­­­­­­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**D. Prior cerebrovascular disease**  \_\_\_ Yes \_\_\_No \_\_Unknown

**If yes, please specify disease:** ­­­­­­­­­­­­­­­­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**E. COLD** \_\_\_ Yes \_\_\_No \_\_Unknown

**F. Connective tissue disease** \_\_\_ Yes \_\_\_No \_\_Unknown

**If yes, please specify disease:** ­­­­­­­­­­­­­­­­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**G. Liver disease** \_\_\_ Yes \_\_\_No \_\_Unknown

**If yes, please specify disease:** ­­­­­­­­­­­­­­­­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**H. Kidney disease** \_\_\_ Yes \_\_\_No \_\_Unknown

**If yes, please specify disease:** ­­­­­­­­­­­­­­­­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**I. Malignant disease** \_\_\_ Yes \_\_\_No \_\_Unknown

**If yes, please specify disease:** ­­­­­­­­­­­­­­­­­­­­\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**J. HIV** \_\_\_ Yes \_\_\_No \_\_Unknown

**Section 4 Cause of death**

**A. Was the death sudden?** \_\_\_ Yes \_\_\_No \_\_Unknown

**B. Was the death unexpected?** \_\_\_ Yes \_\_\_No \_\_Unknown

**C. Please complete the table below by recording all illnesses and conditions (acute and chronic) or injuries that the patient had at time of death**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Illness / Condition / Injury**(text) |  **Date of onset** | **Certainty of diagnosis\*** |
| Definite | Likely | Possible |
| 1 |  |  |  |  |  |
| 2 |  |  |  |  |  |
| 3 |  |  |  |  |  |
| 4 |  |  |  |  |  |
| 5 |  |  |  |  |  |
| 6 |  |  |  |  |  |
| 7 |  |  |  |  |  |
| 8 |  |  |  |  |  |
| 9 |  |  |  |  |  |

**\*Certainty of Diagnosis: Definite=**95-100% certainty, **Likely=**80-95% certainty**, Possible=**50-80% certainty

**D. Brief narrative of the sequence of events leading to death (please include means of diagnosis of illnesses):**

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**E. In summary, the causal relation between conditions leading to death was (complete this section with the corresponding number form table C above):**

1. Condition that directly caused death (immediate cause):\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

2. Due to, or as a consequence of: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

3. Due to, or as a consequence of: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

4. Due to, or as a consequence of (the underlying condition): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Section 5 Post-mortem / Autopsy**

**A. Has autopsy been performed:** \_\_\_ Yes \_\_\_No \_\_Unknown

**CNS** \_\_\_ Yes \_\_\_No \_\_Unknown Describe\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Respiratory organs** \_\_\_ Yes \_\_\_No \_\_Unknown Describe\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Cardiovascular system \_\_\_ Yes \_\_\_No \_\_Unknown Describe\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Gastrointestinal \_\_\_ Yes \_\_\_No \_\_Unknown Describe\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Uro-genital \_\_\_ Yes \_\_\_No \_\_Unknown Describe\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Muscular-skeletal \_\_\_ Yes \_\_\_No \_\_Unknown Describe\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Endocrine glands \_\_\_ Yes \_\_\_No \_\_Unknown Describe\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Did the autopsy reveal any evidence of intoxication \_\_\_ Yes \_\_\_No \_\_Unknown

**Section 6**  **Graft information**

**A. Graft compatibility:**

**ABO identical** \_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

**ABO compatible** \_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

**Pre-transplant donor specific antibody** \_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

**HLA ABC 10/10 match** \_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

**DRB1 match** \_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

**DQB1 match**  \_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

**B. Was there consistently functioning graft up to the time of death?**

**(acute organ failure as a consequence of the terminal illness is not to be included)**

 \_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

**If no, has the graft been removed? (Relevant for kidney transplants only)**

 \_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

Date:

**C. Was there graft-versus-host disease at time of death? (Relevant for HCT patients only)**

\_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

**D. Was there complete remission of the cancer that resulted in the transplantation, at time of death?**

**(Relevant for cancer patients only)**

 \_\_\_ Yes \_\_\_No \_\_Unknown \_\_not relevant

**Section 7 Concomitant infections**

**A. Were there any concomitant infections identified in the month up to the time of death?**

 \_\_\_ Yes \_\_\_No \_\_Unknown

**If yes, please provide details:**

|  |  |  |
| --- | --- | --- |
| **Microbial agent:**(text) | **Specimen**(text) | **Date of first identification** |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

**B. Was there given any anti-microbial therapy?**

\_\_\_ Yes \_\_\_No \_\_Unknown

**If yes, please specify which one(s):**

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**C. Was there resistance to any anti-microbial agents?**

\_\_\_ Yes \_\_\_No \_\_Unknown

 **If yes, please specify which one(s)?**

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Section 8 Laboratory values latest prior to death**

|  |  |  |  |
| --- | --- | --- | --- |
| **Laboratory values** | **Value** | **Unit** | **Date**  |
| Hemoglobin |  |  |  |
| Creatinine |  |  |  |
| ALT |  |  |  |
| Bilirubine  |  |  |  |
| INR |  |  |  |
| Neutrocytes |  |  |  |

**Section 9 Adverse reactions of any type of medical treatment:**

**A. Was the death considered to be related to a medical treatment?**

\_\_\_ Yes \_\_\_No \_\_Unknown

If yes, please specify which one(s)?

|  |  |  |
| --- | --- | --- |
| **Immunosuppressive therapy:**(text) |  **Date of first initiation** | **Certainty of relationship to drug\*** |
| Definite | Likely | Possible |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
| **Other medication:** |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

\***Definite** suspected (95-100% certainty); **Likely** (80-95%); **Possible** (50-80%)

Please provide a brief narrative of the suspected association

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Supplemental digital content 2. Illustrates an online review form.**

**Title: Classification of Death Causes after Transplantation (CLASS): evaluation of methodology and initial results.**

**1. author: Neval Ete Wareham**

**Supplemental digital content 2**

**Section 1 Underlying cause of death and condition contributing to death**

|  |  |  |  |
| --- | --- | --- | --- |
| **Cause of death** | **Ilness/Condition/Injury (text)** | **Code**(1 – 14) | **Certainty\*:** |
| **Definitely** | **Likely** | **Possibly** |
| **Immediate** (Mandatory) |  |  |  |  |  |
| **Contributing** (if applicable) |  |  |  |  |  |
| **Contributing**(if applicable) |  |  |  |  |  |
| **Contributing**(if applicable) |  |  |  |  |  |
| **Contributing**(if applicable) |  |  |  |  |  |
| **Contributing**(if applicable) |  |  |  |  |  |
| **Underlying** (Mandatory) |  |  |  |  |  |

**\*Certainty of Diagnosis: Definite=**95-100% certainty, **Likely=**80-95% certainty**, Possible=**50-80% certainty

**Comments:**

**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

**Section 2 Death considered related to transplantation-specific causes?**

1. Related to the transplantation-related immunosuppressive treatment?

\_\_\_ Yes \_\_\_No \_\_Unknown

1. Related to the perioperational procedures?

\_\_\_ Yes \_\_\_No \_\_Unknown

1. Related to other transplant specific cause?

\_\_\_ Yes \_\_\_No \_\_Unknown

If yes, please specify:

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Supplemental digital content 3. A list with pre-defined categories of death used to classify cause of death in this study.**

**Title: Classification of Death Causes after Transplantation (CLASS): evaluation of methodology and initial results.**

**1. author: Neval Ete Wareham**

**Supplemental digital content 3**

**Classification, List of Causes of Death**

|  |  |
| --- | --- |
| **Disease groups** | **Disease subgroups** |
| 1. **Graft failure**
 | * 1. **Primary non-function**
 |  |
| * 1. **non-specific**
 |  |
| 1. **Graft rejection**
 | * 1. **Acute**
 |  |
| * 1. **Chronic**
 | * + 1. **BOS**
 |
| 1. **GvHD**
 | * 1. **Acute**
 |  |
| * 1. **Chronic**
 | * + 1. **BOS**
 |
| 1. **Infections**
 | * 1. **Bacterial**
 |  |
| * 1. **Fungal**
 |  |
| * 1. **Viral**
 |  |
| * 1. **Protozoal**
 |  |
| * 1. **Other (specify in comment field)**
 |  |
| * 1. **Other infection (specify in comment field)**
 |  |
| * 1. **Unknown etiology**
 |  |
| 1. **Hemorrhage**
 | * 1. **Gastro-intestinal**
 |  |
| * 1. **Ruptures vascular aneurysm**
 |  |
| * 1. **From surgery**
 |  |
| * 1. **Other (specify in comment field)**
 |  |
| 1. **Malignancy**
 | * 1. **De novo**
 | * + 1. **De novo - Lip and oral cavity**
 |
| * + 1. **De novo - Nasal cavity and middle ear**
 |
| * + 1. **De novo - Larynx, trachea, lung, mediastinum and pleura**
 |
| * + 1. **De novo – Thymus**
 |
| * + 1. **De novo – Heart**
 |
| * + 1. **De novo - GI tract**
 |
| * + 1. **De novo - Liver and intrahepatic bile duct**
 |
| * + 1. **De novo – Gallbladder**
 |
| * + 1. **De novo - Other biliary tract**
 |
| * + 1. **De novo – Pancreas**
 |
| * + 1. **De novo – Bone**
 |
| * + 1. **De novo – Skin**
 |
| * + 1. **De novo - Mesothelial and soft tissue**
 |
| * + 1. **De novo - Urogenital system**
 |
| * + 1. **De novo – CNS**
 |
| * + 1. **De novo – Eye**
 |
| * + 1. **De novo - Thyroid gland**
 |
| * + 1. **De novo - Lymphoid and hematopoietic tissue**
 |
| * + 1. **De novo – Mamma**
 |
| * 1. **Relapse**
 | * + 1. **Relapse - Lip and oral cavity**
 |
| * + 1. **Relapse - Nasal cavity and middle ear**
 |
| * + 1. **Relapse - Larynx, trachea, lung, mediastinum and pleura**
 |
| * + 1. **Relapse – Thymus**
 |
| * + 1. **Relapse – Heart**
 |
| * + 1. **Relapse - GI tract**
 |
| * + 1. **- Liver and intrahepatic bile duct**
 |
| * + 1. **Relapse – Gallbladder**
 |
| * + 1. **Relapse - Other biliary tract**
 |
| * + 1. **Relapse – Pancreas**
 |
| * + 1. **Relapse – Bone**
 |
| * + 1. **Relapse – Skin**
 |
| * + 1. **Relapse - Mesothelial and soft tissue**
 |
| * + 1. **Relapse - Urogenital system**
 |
| * + 1. **Relapse – CNS**
 |
| * + 1. **Relapse – Eye**
 |
| * + 1. **Relapse - Thyroid gland**
 |
| * + 1. **Relapse - Lymphoid and hematopoietic tissue**
 |
| * + 1. **Relapse – Mamma**
 |
| * 1. **Progression of underlying malignancy**
 | * + 1. **Cancer progression - Lip and oral cavity**
 |
| * + 1. **Cancer progression - Nasal cavity and middle ear**
 |
| * + 1. **Cancer progression - Larynx, trachea, lung, mediastinum and pleura**
 |
| * + 1. **Cancer progression – Thymus**
 |
| * + 1. **Cancer progression – Heart**
 |
| * + 1. **Cancer progression - GI tract**
 |
| * + 1. **Cancer progression - Liver and intrahepatic bile duct**
 |
| * + 1. **Cancer progression – Gallbladder**
 |
| * + 1. **Cancer progression - Other biliary tract**
 |
| * + 1. **Cancer progression – Pancreas**
 |
| * + 1. **Cancer progression – Bone**
 |
| * + 1. **Cancer progression – Skin**
 |
| * + 1. **Cancer progression - Mesothelial and soft tissue**
 |
| * + 1. **Cancer progression - Urogenital system**
 |
| * + 1. **Cancer progression – CNS**
 |
| * + 1. **Cancer progression – Eye**
 |
| * + 1. **Cancer progression - Thyroid gland**
 |
| * + 1. **Cancer progression - Lymphoid and hematopoietic tissue**
 |
| * + 1. **Cancer progression – Mamma**
 |
| * 1. **Secondary cancer**
 | * + 1. **Lip and oral cavity**
 |
| * + 1. **Secondary cancer - Nasal cavity and middle ear**
 |
| * + 1. **Secondary cancer - Larynx, trachea, lung, mediastinum and pleura**
 |
| * + 1. **Secondary cancer – Thymus**
 |
| * + 1. **Secondary cancer – Heart**
 |
| * + 1. **Secondary cancer - GI tract**
 |
| * + 1. **Secondary cancer - Liver and intrahepatic bile duct**
 |
| * + 1. **Secondary cancer – Gallbladder**
 |
| * + 1. **Secondary cancer - Other biliary tract**
 |
| * + 1. **Secondary cancer – Pancreas**
 |
| * + 1. **Secondary cancer – Bone**
 |
| * + 1. **Secondary cancer – Skin**
 |
| * + 1. **Secondary cancer - Mesothelial and soft tissue**
 |
| * + 1. **Secondary cancer - Urogenital system**
 |
| * + 1. **Secondary cancer – CNS**
 |
| * + 1. **Secondary cancer – Eye**
 |
| * + 1. **Secondary cancer - Thyroid gland**
 |
| * + 1. **Secondary cancer - Lymphoid and hematopoietic tissue**
 |
| * + 1. **Secondary cancer – Mamma**
 |
| 1. **Organ failure or dysfunction**

**(not due to graft rejection, graft failure, GvHD, infection, or cancer)** | * 1. **Liver**
 | * + 1. **Due to drug toxicity**
 |
| * + 1. **Cirrhosis - not viral**
 |
| * + 1. **Cystic liver disease**
 |
| * + 1. **VOD**
 |
| * + 1. **Liver failure - cause unknown**
 |
| * 1. **Cardiac or vascular**
 | * + 1. **Myocardial ischemia and infarction**
 |
| * + 1. **Hemorrhagic pericarditis**
 |
| * + 1. **Other causes of cardiac failure (specify in comment field)**
 |
| * + 1. **Fluid overload**
 |
| * + 1. **Pulmonary embolus**
 |
| * + 1. **Cerebrovascular accident**
 |
| * + 1. **Mesenteric infarction**
 |
| * + 1. **Transplant-associated thrombocytic microangiopathy (TAM)**
 |
| * 1. **Pulmonary**
 | * + 1. **BOS**
 |
| * + 1. **COLD**
 |
| * + 1. **Other (specify in comment field)**
 |
| * 1. **CNS**
 |  |
| * 1. **Renal**
 | * + 1. **Acute**
 |
| * + 1. **Chronic**
 |
| * 1. **GI tract**
 |  |
| * 1. **Pancreas**
 | * + 1. **Pancreatitis**
 |
| * + 1. **Other (specify in comment field)**
 |
| * 1. **Multi-organ failure**
 |  |
| * 1. **Hematological disease**
 |  |
| * 1. **Endocrine disease**
 |  |
| * 1. **DM**
 |  |
| * 1. **Psychiatric disease**
 |  |
| * 1. **Skin and motor system**
 |  |
| * 1. **Urogenital disease**
 |  |
| * 1. **Obstetric complications**
 |  |
| * 1. **Congenital disorders**
 |  |
| * 1. **Connective tissue disease**
 |  |
| * 1. **Other organ failure or dysfunction (specify in comment field)**
 |  |
| 1. **Substance abuse**
 | * + 1. **Chronic alcohol abuse**
 |  |
| * + 1. **Chronic intravenous drug-use**
 |  |
| * + 1. **Acute intoxication**
 |  |
| 1. **Withdrawal of active treatment**
 | * 1. **The patients initiative**
 |  |
| * 1. **The clinicians initiative**
 |
| 1. **Accidental death**
 |  |  |
| 1. **Suicide**
 |  |  |
| 1. **Other causes (specify in comment field)**
 |  |  |
| 1. **Unclassifiable causes**
 |  |  |
| 1. **Unknown**
 |  |  |

**\*** The classification algorithm for defining cause of death was conditional and thus certain causes of death had a higher weight compared to others. For example if primary graft failure, graft rejection, graft versus host disease, infection or malignancy were present at time of death and initiated the train of morbid events that lead to death, then these were assigned as the underlying cause of death whereas contributing and immediate causes were recorded with one of the other appropriate categories. If more than one cause with the highest weight were present at time of death, then the sequence in time and the extent of contribution to the fatal outcome would determine which cause was recorded as underlying and which as contributing or immediate cause of death. If none of the aforementioned were recorded as the underlying cause of death, then the algorithm continued with hemorrhage, organ specific dysfunctions, etc.

**Supplemental digital content 4. For comparison between the Danish National Death Cause registry and the 14 specific categories included in our classification algorithm, these categories were assigned a corresponding ICD-10. This is illustrated in this document.**

**Title: Classification of Death Causes after Transplantation (CLASS): evaluation of methodology and initial results.**

**1. author: Neval Ete Wareham**

**Supplemental digital content 4**

**International Classification of Diseases, 10th revision and Classification of Death Causes after Transplantation included in each disease group category.**

|  |  |
| --- | --- |
| **CLASS code** | **ICD-10** |
| **1. Graft failure****2. Graft rejection****3. GvHD** | **T82, T83, T84, T85, T86, N165** |
| **4. Infection**  | **A00–A019, A03–A072, A078–A09, A20–A28,****A32–A563, A568–A811, A813–A99, B01–B09,****B25–B370, B372–B382, B39–B392, B40–B450,****B46–B581, B583, B99, G00–G02, J12–J18** |
| **5. Hemorrhage1** | **R58** |
| **6. Malignancy** | **C00-C96** |
| **7.1. Liver** | **B15–B19, K65, K70–K77, K922** |
| **7.2. Cardiac or vascular** | **I00–I45, I47–I99** |
| **7.3. Pulmonary** | **J40–J99** |
| **7.4 CNS** | **G048-G99** |
| **7.5 Renal** | **N00-N29** |
| **7.6 GI tract** | **K00-K66, K80-K83, K87-K93** |
| **7.7 Pancreas** | **E16, K85-K87** |
| **7.8. Multi-organ failure** | **-** |
| **7.9 Hematological disease** | **D50–D89** |
| **7.10. Endocrine disease** | **E15-E90** |
| **7.11 Diabetes Mellitus** | **E10-E14** |
| **7. 12 Psychiatric disease** | **F00-F99** |
| **7.13 Skin and motor system** | **L00-L99, M00-M25, M40-M99** |
| **7.14. Urogenital disease** | **N30-N99** |
| **7.15. Obstetric complications** | **O00-O99** |
| **7.16. Congenital disorders** | **Q00-Q99** |
| **7.17. Connective tissue disease** | **M30-M36** |
| **7.18. Other organ failure or dysfunction****12. Other causes** | **Any other code** |
| **8. Substance abuse** | **F10-F19, T36–T65** |
| **9. Withdrawal of active treatment** | **-** |
| **10. Accidental death** | **DX60-DY09** |
| **11. Suicide** | **X60–X84** |
| **13. Unclassifiable causes****14. Unknown** | **R092, R95, R960–R961, R98, R99** |

1ICD10 codes for organ disease together with hemorrhage corresponded to the CLASS code for hemorrhage with the exception of hemorrhage from the central nervous system which corresponded to the CLASS code 7.4.

**Supplemental digital content 5. The recorded underlying cause of death, according to transplant type (solid organ and hematopoietic stem cell transplantation).**

**Title: Classification of Death Causes after Transplantation (CLASS): evaluation of methodology and initial results.**

**1. author: Neval Ete Wareham**

**Supplemental digital content 5**

Abbreviations: SOT; solid organ transplantation, HSCT; hematopoietic stem cell transplantation.